What is claimed is :

1. A composition for the predictive diagnosis of an hepatocellular carcinoma in a patient comprising at least a polynucleotide containing a DNA marker which is localized in the following chromosomal regions :

a) 1p;
b) 1q;
c) 2q;
d) 4q;
e) 6p;
f) 7p;
g) 7q;
h) 8p;
i) 8q;
j) 9p;
k) 9q;
l) 10q;
m) 13q;
n) 14q;
o) 16p;
p) 16q;
q) 17p;
r) 17q.

said DNA markers any of the publicly available markers spanning these specific chromosomal loci of interrest, namely, microsatellite DNA markers, namely :

1) Microsatellite DNA markers;
2) RFLP markers;
3) VNTR markers (Varaiable Number of Tandem Repeats);
4) STSs markers (Simple Tag Sequences);
5) ESTs (Expressed sequence Tags).

2. The composition of claim 1 comprising at least a polynucleotide containing a DNA marker which is preferably localized in the following chromosomal regions :

a) 8p23;
b) 8p122;
c) 8p21;

d) 1p35-p36;
e) 16q23-q24 and
f) 14q32,
said DNA markers any of the publicly available markers spanning these specific chromosomal loci of interrest, namely, microsatellite DNA markers, namely :
1) Microsatellite DNA markers;
2) RFLP markers;
3)VNTR markers (Varaiable Number of Tandem Repeats);
4) STSs markers (Simple Tag Sequences);
5) ESTs (Expressed sequence Tags).

3. The diagnostic composition of claim 1 or 2 comprising at least one polynucleotide of the two nucleic acid molecules constituting the pair of primers of at least one microsatellite DNA marker choosen among the following microsatellite DNA markers :

a) 1p : D1S243, D1S214, D1S228, D1S199, D1S255, D1S476, D1S198, D1S207, D1S248, D1S436, D1S2644, D1S199, D1S2843, D1S478, D1S2828, D1S2902, D1S247 and D1S255;
b) 1q : D1S305, D1S196, D1S238, D1S249, D1S229, D1S235 and D1S304;
c) 2q : D2S113, D2S347, D2S151, D2S294, D2S311, D2S143, D2S159 and D2S125;
d) 4q : D4S392, D4S1538, D4S1578, D4S406, D4S430, D4S422, D4S1548, D4S1597, D4S408, D4S426, D4S3042, D4S2922, D4S400, D4S395, D4S1534, D4S2929, D4S2460, D4S1572, D4S1564, D4S2945, D4S1616, D4S2937, D4S1613 and D4S427;
e) 6p : D6S344, D6S309, D6S260, D6S276, D6S426 and D6S294;
f) 7p : D7S531, D7S664, D7S493, D7S484 and D7S519;
g) 7q : D7S669, D7S657, D7S486, D7S495, D7S483 and D7S550;
h) 8p : D8S277, D8S550, D8S282, D8S283 and D8S260, D8S264, D8S262, D8S1140, D8S518, D8S1099, D8S1742, D8S561, D8S1819, D8S1469, D8S1721, D8S552, D8S1731, D8S261, D8S1752, D8S1771, D8S1820, D8S532 and D8S285;
i) 8q : D8S273, D8S281 and D8S272;
j) 9p : D9S288, D9S156, D9S161 and D9S273;
k) 9q : D9S153, D9S277, D9S195, D9S164 and D9S158;
l) 10q : D10S589, D10S185, D10S597, D10S587 and D10S212;
m) 13q : D13S175, D13S171, D13S284, D13S170, D13S158, D13S285 and D13S286;

n) 14q : D14S261, D14S75, D14S63, D14S74, D14S292, D14S81, D14S280, D14S995, D14S977, D14S1062 and D14S265;
o) 16p : D16S521, D16S407, D16S420 and D16S411;
p) 16q : D16S408, D16S518, D16S422 and D16S520, D16S507, D16S3098, D16S505, D16S511, D16S422 and D16S402;
q) 17p : D17S926, D17S86 and D17S953;
r) 17q : D17S933, D17S787, D17S949, D17S784 and D17S928;

4. The diagnostic composition according to claim 3 comprising at least two polynucleotides choosen among the nucleic acid molecules constituting the pair of primers of a microsatelllite DNA markers of groups a) to r), providing that said polynucleotides do not belong to the same pair of primers defining said DNA marker.

5. The diagnostic composition according to claim 3 or 4 wherein the polynucleotide molecules are choosen among the following microsatellite DNA markers :
D4S426, D6S305, D7S493, D8S227, D13S284 and D17S786.

6. The diagnostic composition according to claim 3 or 4 wherein the polynucleotide molecules are choosen among the following microsatellite DNA markers :
D1S238, D1S235, D2S336, D2S125, D7S495, D8S263, D9S273, D9S164, D14S81 and D17S928.

7. The diagnostic composition according to claim 3 or 4 wherein the polynucleotide molecules are choosen among the following microsatellite DNA markers :
D8S1742, D8S1469, D8S1731, D8S1752, D1S2644, D1S199, D1S478, D1S2828, D1S247, D1S255, D14S280, D14S995, D14S81, D14S265, D14S292, D16S3098, D16S505, D16S511, D16S422 and D16S402.

8. The diagnostic composition according to claim 3 or 4 wherein the polynucleotide molecules are choosen among the following microsatellite DNA markers :
D8S264, D8S262, D8S518, D8S1742, D8S277, D8S1819, D8S1721, D8S1731, D8S1752.

9. The diagnostic composition according to claim 3 or 4 wherein the polynucleotide molecules are choosen among the following microsatellite DNA markers :

D1S436, D1S2644, D1S199, D1S478, D1S2828, D1S247 and D1S255.

10. The diagnostic composition according to claim 3 or 4 wherein the polynucleotide molecules are choosen among the following microsatellite DNA markers : D16S3098, D16S505, D16S511, D16S422 and D16S402.

11. The diagnostic composition according to claim 3 or 4 wherein the polynucleotide molecules are choosen among the following microsatellite DNA markers : D14S280, D14S81and D14S265.

12. The diagnostic composition according to claim 3 or 4 wherein the polynucleotide molecules are choosen among the following microsatellite DNA markers : D4S400, D4S1572, D4S1564, D4S2945, D4S1616 and D4S2937

13. The diagnostic composition according to claim 3 or 4 wherein the polynucleotide molecules choosen among the DNA markers are used in the following combinations:
a) markers of 1p, choosen among D1S243, D1S214, D1S228, D1S199, D1S2155, D1S476, D1S198, D1S207 and D1S248, with markers of 13q, choosen among D13S175, D13SD13S171, D13S284, D13S170, D13S158, D13S285 and D13S286;
b) markers of 1p, choosen among D1S243, D1S214, D1S228, D1S199, D1S2155, D1S476, D1S198. D1S207 and D1S248 with markers of 8p, choosen among D8S264, D8S262, D8S518, D8S1742, D8S277, D8S1819, D8S1721, D8S1731, D8S1752;
c) markers of 6q, choosen among D6S462, D6S261, D6S292, D6S290, D6S305, D6S426 and D6S294 with markers of 13q, choosen among D13S175, D13S171, D13S284, D13S170, D13S158, D13S285 and D13S286.

14. The diagnostic composition according to claim 3 or 4 wherein the polynucleotide molecules choosen among the DNA markers are used in the following combinations:
a) Microstallite markers of 16p, choosen among D16S521, D16S407, D16S420 and D16S411;
b) Microsatellite markers of 17p, choosen among D17S933, D17S787, D17S949, D17S784 and D17S928,

15. A diagnostic method for the predictive prognosis of HCC in a patient comprising the following steps :

a) Preparing two tissue samples from a patient, the first tissue sample being derived from an organ different than the liver and the second tissue sample being derived from the liver of said patient;
b) Optionally making the genomic DNA contained in the cells of the tissue samples of step a) available to hybridization;
c) Amplifying the genomic DNA of step b) with at least one microsatellite DNA marker choosen among the markers of groups a) to r) of claim 3 or a composition containing a combination of said DNA markers;
d) detecting the alterations that have occurred by comparing the resulting amplified products of step c) derived respectively from the first and the second tissue sample.

16. The diagnostic method of claim 14 wherein in step d) it is made use of at least one of the primers constituting the amplifying tools of step c) as oligonuleotide probes (detection tools), said probes being preferentially radioactively or non-radioactively labelled.

17. A method for isolating and /or purifying a tumor suppressor gene polynucleotide involved in the occurrence of a HCC in a patient comprising the steps of :
a) Constructing a cosmid library from a selected YAC clone;
b) Selecting cosmid clones of interest by colony hybridizattion with labelled human genomic DNA as a probe;
c) Constructing a contig map of the purified selected cosmid clones;
d) Performing an exon amplification reaction and inserting the reverse transcribed RNA fragments in a suitable vector;
e) Hybridizing the inserts of step d) with a suitable human cDNA library, preferably a fetal or adult liver cDNA library and selecting the hybridizable cDNA clones;
f) Sequencing the selected cDNA clones inserts and characterizing the coding sequences;

18. A tumor suppressor gene polynucleotide involved in the occurrence of a HCC in a patient obtained according to the method of claim 17.

19. A fragment of the polynucleotide of claim 18 obtained by restriction enzyme cleavage or chemical synthesis.

20. The polynucleotide or polynucleotide fragment according to anyone of claims 18 or 19, which is an oligonucleotide probe or primer.

21. A method for detecting a genetic abnormality linked to the HCC in a biological sample containing DNA or cDNA, comprising the steps of :

a) bringing the biological sample into contact with a pair of oligonucleotide fragments according to claim 20, the DNA contained in the sample having been optionally made available to hybridization and under conditions permitting a hybridization of the said oligonucleotide fragments with the DNA contained in the biological sample;

b) amplifying the DNA

c) revealing the amplification products;

d) optionally detecting a mutation or a deletion by appropriate techniques.

22. The method of claim 21 wherein step d) consists in a detection method choosen among the followings :

Single Strand Polymorphism, Band Shift Assay, Restriction Site Analysis, Allele Specific Oligonucleotide Assay, Allele-specific priming, Heteroduplex Analysis, Denaturing Gel Electrophoresis, Chemical Cleavage Method, Fluorescence Activated Mismatch Analysis.

23. A method for detecting a genetic abnormality linked to the HCC in a biological sample containing DNA or cDNA, comprising the steps of :

a) bringing the biological sample into contact with an oligonucleotide probe according to claim 20, the DNA contained in the sample having been optionally made available to hybridization and under conditions permitting a hybridization of the primers with the DNA contained in the biological sample;

b) detecting the hybrid formed between the oligonucleotide probe and the DNA contained in the biological sample.

24. A method for detecting a genetic abnormality linked to the HCC in a biological sample containing DNA, comprising the steps of :

a) bringing into contact a first oligonucleotide probe according to claim 20 that has been immobilized on a suuport, the DNA contained in the sample having

been optionally made available to hybridization and under conditions permitting a hybridization of the primers with the DNA contained in the biological sample;

b) bringing into contact the hybrid formed between the immobilized first oligonucleotide probe and the DNA contained in the biological sample with a second oligonucleotide probe according to claim 19, which second probe hybridizes with a sequence different from the sequence to which the immobilized first probe hybridizes, optionally after having removed the DNA contained in the biological sample which has not hybridized with the immobilized first oligonucleotide probe.

25. A method for detecting a genetic abnormality linked to the HCC in a biological sample containing DNA, by the detection of the presence and of the position of base substitutions or base deletions in a nucleotide sequence included in a double stranded DNA preparation to be tested, the said method comprising the steps of :

a) amplifying specifically the region containing, on one hand, the nucleotide sequence of the DNA to be tested and on the other hand the nucleotide sequence of a DNA of known sequence, the DNA of known sequence being a polynucleotide according to the invention;

b) labelling the sense and antisense strands of these DNA with diferent fluorescent or other non-isotopic labels;

c) hybridizing the amplified DNAs;

d) revealing the heteroduplex formed between the DNA of known sequence and

26. A diagnostic kit for the detection of a genetic abnormality linked to the HCC in a biological sample, comprising the following elements :

a) a pair of oligonucleotides according to claim 20 ;

b) the reagents necessary for carrying out a DNA amplification;

c) a component which makes it possible to determine the length of the amplified fragments or to detect a mutation.

27. A method for the producing a polypeptide encoded by a candidate tumor suppressor gene according to claim 19, the said method comprising the steps of :

a) Optionally amplifying the nucleic acid coding for the desired polypeptide using a pair of primers according to the invention (by SDA, TAS, 3SR NASBA, TMA etc.).

b) Inserting the nucleic acid of interest in an appropriate vector;

c) culturing, in an appropriate culture medium, a cell host previously transformed or transfected with the recombinant vector of step b);
d) harvesting the culture medium thus conditioned or lyse the cell host, for example by sonication or by an osmotic shock;
e) separating or purifying, from the said culture medium, or from the pellet of the resultant host cell lysate the thus produced polypeptide of interest.
f) Characterizing the produced polypeptide of interest.